





# Persistent ENT Manifestations in Individuals who Recovered from COVID-19: A Systematic Review

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## Abstract

**Introduction** Long coronavirus disease (COVID) refers to the persistence of symptoms long after the recovery from the acute phase of the illness, and it is due to the interplay of various inflammatory mechanisms. This has led to emergence of new deficits, including otorhinolaryngological symptoms, in patients who have recovered from COVID. The plethora of otorhinolaryngological symptoms associated with long COVID are tinnitus, sensorineural hearing loss (SNHL), vertigo, nasal congestion, sinonasal discomfort, hyposmia/anosmia, dysgeusia, sore throat, dry cough, dyspnea, dysphagia, and hoarseness of voice.

**Objective** To evaluate the possible ENT symptoms in patients who have recovered from COVID and to combine those findings with our experience.

**Data Synthesis** We conducted a search on the PubMed, ENT Cochrane, Web of Science, and Google Scholar databases, and a total of 44 studies were selected for the present review.

**Conclusion** Otorhinolaryngological complications such as tinnitus, SNHL, vertigo, nasal congestion, sinonasal discomfort, hyposmia/anosmia, dysgeusia, sore throat, dry cough, dyspnea, dysphagia, and hoarseness of voice have been widely reported among in long-COVID patients.

## Keywords

- ▶ long COVID
- ▶ SARS-CoV-2
- ▶ otorhinolaryngological manifestations

## Introduction

In December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) originated in Wuhan, China.<sup>1</sup> On March 11, 2020, due to its unprecedented global spread, the World Health Organization (WHO) labelled coronavirus disease 2019 (COVID-19), the infection caused by SARS-CoV-2, a pandemic.<sup>2</sup> It is a very aggressive and contagious illness that spreads mostly by aerosols and respiratory droplets.<sup>3</sup> The primary entry points for the virus are the nasal and oral cavities, with the nasal cavity and nasopharynx being the

most common sites for viral replication. The virus binds to the angiotensin-converting enzyme 2 (ACE2) receptor and initiates an inflammatory cascade with multisystem involvement.<sup>4–6</sup> The symptoms may range from minor ailments to life-threatening complications. In addition to symptoms of the lower respiratory tract, such as cough, fever, and dyspnea, extrapulmonary symptoms affecting the ear, nose, and throat are also often observed.<sup>7</sup>

It has been observed that most SARS-CoV-2-positive patients did not require any hospitalization and

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presented with mild or no symptoms. Among these mild symptoms, alterations in the senses of smell and taste have been observed to occur early.<sup>8</sup>

While some of the symptoms diminish with time, others have catastrophic long-term effects that persist even after recovery from the acute infection, resulting in death or significant impairment of functions. “Long COVID” or “post-COVID syndrome” refers to this unusual and unexpected persistence of symptoms long after recovery from the initial illness.<sup>9</sup> Long COVID is associated with a plethora of otorhinolaryngological symptoms, including tinnitus, sensorineural hearing loss (SNHL), vertigo, nasal congestion, sinonasal discomfort, hyposmia/anosmia, dysgeusia, sore throat, dry cough, dyspnea, dysphagia, and hoarseness of voice.

## Methods

We conducted a search on the PubMed, ENT Cochrane, Web of Science, and Google Scholar databases without restrictions regarding the time of publication of the articles, with an emphasis on the most recent reports, using the terms *COVID-19*, *long COVID*, and *otorhinolaryngological manifestation or ENT symptoms*. Boolean operators (AND, NOT, and OR) were used to restrict and extend the search. Long COVID can refer to certain symptoms that seem to persist (from three to nine months or longer) in an individual who has recovered from COVID-19.<sup>10</sup> However, some authors<sup>11</sup> also believe these symptoms can persist for years.

Initially, 462 articles were retrieved based on our search parameters. Out of these, 392 publications were excluded, as they were not found to be relevant to the topic in question. Consequently, a total of 70 studies were selected for the present review. The purpose of the current article is to compile the broad spectrum of ear, nose, and throat (ENT) presentations of long COVID and to highlight the diagnosis based on the available literature combined with our experience.

## Review of the Literature

### Otological Symptoms after COVID-19

We analyzed 25 articles in detail to highlight the symptoms and treatment of the otological symptoms of long COVID exclusively. Combined, the data from these studies revealed that out of 1,000 patients who have recovered from COVID, 80 (8%) presented with SNHL, 140 (14%), with tinnitus, 142 (14.2%), with vertigo, 2 (0.2%), with facial paralysis, 19 (1.9%), with an earache, and 58 (5.81%) presented with aural fullness. The broad spectrum of ear symptoms after recovery from COVID are hearing loss, tinnitus, vertigo, facial palsy, earache, and aural fullness.<sup>12–36</sup>

At our center, approximately 22 patients reported to us with symptoms of hearing loss, tinnitus and aural fullness; 4 out of them presented with tinnitus along with hearing loss, 14, with hearing loss without any other symptoms, and 4, with aural fullness. These patients are still being treated and are under follow-up.

### Nasal and Associated Chemosensory Deficit Symptoms Following COVID-19

We analyzed 11 studies in detail to conclude that the most common nasal and associated chemosensory deficit symptoms are smell and taste dysfunctions, such as phantosmia, parosmia, hyposmia, anosmia, phantogeusia, parageusia, ageusia, or rhinitis symptoms, such as nasal discharge, nasal blockage, and sinonasal pain.<sup>33,34,36–43</sup>

In each study, the authors observed chemosensory deficit symptoms, including dysfunctions in the senses of smell and taste in 861 patients (31.22%) out of a total of 2,757 patients who have recovered from COVID. Six<sup>33,34,37,40,41,43</sup> out of 10 studies identified rhinitis symptoms in 385 (19.63%) of a total 1,961 patients.

In 2022, Bianco et al.<sup>44</sup> conducted a prospective study on 76 patients for an objective assessment of olfactory function, which revealed that 48 (63.16%) patients had recovered completely, 26 (34.21%) were hyposmic, and 2 (2.63%) were anosmic. The authors reported<sup>44</sup> that the duration of the SARS-CoV-2 infection was observed to be more severe among individuals who did not regain their sense of smell. Hence, they could safely conclude that the duration of the infection negatively correlates with the recovery of olfactory function.

A total of four patients presented to the ENT Outpatient Department (OPD) at our center with nasal complications of long COVID. While 3 out of 4 patients reported with hyposmia, 1 presented with complaints of anosmia. These patients are still under follow up.

### Throat and Laryngeal Symptoms after COVID-19

A total of 10 studies were taken into consideration in order to ascertain that the most prevalent throat and laryngeal symptoms include hoarseness of voice, sore throat, dry throat, trouble swallowing, dyspnea, and cough.<sup>34,36,39,43,45–49</sup>

Out of the 1,826 subjects who have recovered from COVID included in these studies, symptoms of hoarseness of voice were observed in 110 patients (6.02%), sore throat, in 214 (11.72%), dry throat, in 26 (1.42%), difficulty in swallowing in 33 (1.81%), dyspnea, in 313 (17.14%), and cough, in 344 patients (18.84%).

In 4 out of 10 studies,<sup>45,46,48,49</sup> the authors also reported history of intubation, accounting for 52 of 207 (25.12%) patients who had recovered from COVID.

At our center, we have only observed one patient with a finding of vocal cord paresis. We have not observed any other laryngeal complications of long COVID.

## Discussion

The infection by SARS-CoV-2 (COVID-19) is a highly contagious illness with catastrophic effects, which has caused great mortality and morbidity on a global scale. About 80% of the afflicted patients presented with mild to moderate disease, whereas 5% of the cases were considered critical.<sup>50</sup> Long COVID or post-COVID refers to the persistence of many symptoms weeks or months after the infection by SARS-CoV-2, regardless of the viral state.<sup>51</sup> Long-term COVID may be

ongoing or have a relapsing, remitting nature.<sup>52</sup> There may be a continuation of one or more acute COVID symptoms, or the emergence of new symptoms. Most individuals with post-COVID syndrome are polymerase chain reaction (PCR) negative, which indicates recovery of the virus. The lag between microbiological and clinical recovery is referred to as post-COVID syndrome.<sup>53</sup> Most long-term COVID patients recover biochemically and radiologically.<sup>54</sup>

Long COVID may be caused by the persistence of inflammatory process or immune response/autoantibody production, the persistence of the virus in the body, the sequelae of organ dysfunction, and the varying time involved for the regeneration of each organ, postintensive care syndrome, complications due to the COVID infection or complications due to underlying diseases or adverse effects of the medications used. Therefore, multiple pathways contribute to the development of long COVID in various patients.<sup>55,56</sup> Long COVID patients commonly experience extreme fatigue, shortness of breath, cough, chest discomfort, palpitations, headache, joint pain, muscle ache and fatigue, insomnia, diarrhea, poor balance and gait, neurocognitive disorders such as memory and attention problems, and a decline in quality of life.<sup>57</sup>

Tinnitus, SNHL, vertigo, facial paralysis, earache, aural fullness, gustatory and olfactory dysfunctions, rhinitis symptoms such as nasal discharge and nasal obstruction, dyspnea, cough, hoarseness of voice, dysphagia, sore throat, and dry throat are otorhinolaryngological symptoms of long COVID. based on these symptoms, neuro-otorhinolaryngological symptoms can be explained through various mechanisms. This might be due to hypoxia caused by respiratory failure, immune-mediated injury, coagulation problems, or direct viral invasion.<sup>58</sup>

The SARS-Cov-2 virus can also cause direct damage by binding to the ACE2 receptor, which is commonly expressed in the nasal, laryngeal, or tracheal tracts, as well as in the neuro-olfactory epithelium, the lungs, the Eustachian tube, the middle ear, the cochlear hair cells, the oral cavity, including the taste buds, the endothelium of blood vessels, and the thyroid gland. This virus may directly infiltrate tissue and, since it is neuroinvasive and neurotrophic, it can cause axonal transport, thus causing long-term damage to individual neurons. Involvement of the nasal, laryngeal, and tracheal tracts, as well as the neuro-olfactory epithelium, results in rhinitis, anosmia, sore throat, dry throat, dysphagia, hoarseness of voice, and cough. Involvement of the lungs results in dyspnea, hypoxic symptoms, and hemoptysis.

Involvement of the Eustachian tube and middle ear causes earache and aural fullness. The combination of cochlear hair cells with the involvement of the vestibulocochlear nerve and facial nerve results in cochlear neuritis/labyrinthitis or vestibular neuritis, hence further adding to the symptoms of SNHL, tinnitus, vertigo, and facial nerve paralysis. Involvement of the oral cavity, including the taste buds, results in gustatory impairment. Due to the predilection of the virus for the thyroid gland through the ACE 2 receptors, thyroid involvement results in subacute thyroiditis.<sup>59-62</sup>

Involvement of terminal cochlear artery supply resulting in SNHL and tinnitus, as a result of indirect ischemia injury, is

another possible cause of audiovestibular symptoms. There is degradation of the basal lamina of endothelial cells, congestion of blood vessels, and an infiltration of macrophages, astrocytes, and lymphocytes around the blood vessels. This also causes microhemorrhages in the parenchyma and labyrinth of the brain.<sup>17,19,63</sup> There is an aberrant immune response characterized by the formation of a significant number of autoantibodies directed against blood vessels, which may lead to autoimmune thrombocytopenia and the subsequent development of labyrinthine ischemia due to hypoxia.<sup>64,65</sup>

In the etiopathogenesis of neuro-otorhinolaryngological symptoms, inflammatory cytokines and their overproduction also play a role. Their excessive production is the cause of chronic symptoms. Interleukin 6 generated by the lymphocytes, the fibroblasts, and the bronchial epithelium during SARS-CoV-2 infection may control synaptic plasticity, alter cerebral blood flow, and induce neuroinflammation.<sup>66,67</sup>

In addition to the aforementioned processes, the use of ototoxic medicines such as hydroxychloroquine, favipiravir, azithromycin, and furosemide to treat COVID might result in reversible or irreversible hearing impairment.<sup>68-71</sup>

In our opinion, the treatment for the otorhinolaryngological symptoms of long-term COVID requires a multidisciplinary strategy that includes examination, symptomatic therapy, treatment of underlying issues, and long-term monitoring of ongoing symptoms for the identification and timely intervention regarding the complications.

Monitored steroids at a low dose can be used for the treatment of the inflammatory processes such as neuroinflammation. However, steroids must be administered with caution and after taking complete medical history of the patient in detail. The uncontrolled and injudicious use of steroids is has also been observed to result in sequelae like mucormycosis in long-COVID patients.

## Conclusion

Numerous complications of long COVID have been reported in the literature, with ENT complications contributing greatly to the impact on the lives of patients after the pandemic. We have observed that otorhinolaryngological complications, such as tinnitus, SNHL, vertigo, nasal congestion, sinonasal discomfort, hyposmia/anosmia, dysgeusia, sore throat, dry cough, dyspnea, dysphagia, hoarseness of voice, and hypothyroidism have been widely reported. We believe that although “wait and watch” is the immediate answer to any mild complaint, steroids and nootropic medicines might play some role in the treatment of certain complications mentioned in the present review. However, a detailed medical history and adequate dosage and duration of medication use are the mainstay of the management of most ENT complications of long COVID.

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### Conflict of Interests

The authors have no conflict of interest to declare.

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